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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
PITRAK, JENNIFER S	

ART UNIT	PAPER NUMBER
1635	

MAIL DATE	DELIVERY MODE
12/17/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/551,466	JEONG ET AL.	
	Examiner	Art Unit	
	JENNIFER PITRAK	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10/01/2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4 and 6-14* is/are pending in the application.

4a) Of the above claim(s) *11-14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4 and 6-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Remarks

The arguments filed 10/01/2010 have been entered and considered. Claims 1-4 and 6-14 are pending. Claims 11-14 are withdrawn. Claims 1-4 and 6-10 are under examination. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 103 - Maintained

Hoffman, et al.

Claims 1, 2, 4, 6, 7, 9, and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hoffman, et al. (US Patent 7,737,108, filed 01/05/2001). This rejection is maintained.

The claims are directed to a conjugate for gene transfer wherein the conjugate comprises an antisense oligonucleotide and a hydrophilic polymer, such as PEG, wherein the polymer is covalently attached to the end of the oligonucleotide by an acetal bond. Claims 9 and 10 are directed to a product-by-process wherein the product is the same as that claimed in claim 1, an antisense oligonucleotide-polymer conjugate.

Hoffman, et al. teach antisense oligodeoxynucleotides linked to a hydrophilic polymer such as PEG by an acetal bond (column 4, lines 27-34 and lines 46-51). Oligodeoxynucleotides comprise deoxyribonucleosides linked by phosphodiester bonds. Hoffman, et al. exemplify the use of PEG having a molecular weight of 5kD (column 21, lines 66-67). Hoffman, et al. do not

specifically teach that the polymer is attached to an end of the oligonucleotide or that the polymer conjugated to the oligonucleotide has a molecular weight of over 500 Daltons.

It would have been obvious to one of skill in the art at the time of the instant invention to make an antisense oligonucleotide conjugated to PEG via an acetal bond because Hoffman, et al. teach such a conjugate. It would have been obvious to attach the PEG to an end of the oligonucleotide because the ends of the oligonucleotide are free (i.e., not attached to another nucleotide). It further would have been obvious to use PEG that has a molecular weight that is greater than 500 Daltons because Hoffman, et al. exemplify the use of PEG having a molecular weight of 5000 Daltons. Therefore, the claims would have been obvious at the time the instant invention was made.

Response to arguments

Applicant argues that a prima facie case of obviousness has not been established. In support for this argument, Applicant states that Hoffman reports a composition comprising a hydrophobic polymer and optionally, the hydrophobic polymer can be coupled to a hydrophilic polymer (see page 3 of 10/01/2010 response). Applicant concludes that this teaching of Hoffman indicates that if a hydrophilic polymer is present, it must be coupled to the hydrophobic polymer. Applicant continues, pointing to specific sections of the reference that teach hydrophilic and hydrophobic polymers in the same composition and wherein the hydrophobic component was linked to the hydrophilic component. Applicant concludes that because the composition of Hoffman requires a hydrophobic component and the hydrophilic component is optional, the Hoffman composition is distinct from the instantly claimed composition and also has a distinct mechanism of action from that of the instantly claimed composition, such that one

of skill in the art could not have looked to Hoffman and predicted the result of the present invention (paragraph spanning pages 3 and 4 of 10/01/2010 response). This is not persuasive.

As a first matter, the instant claims do no exclude a hydrophobic component. Therefore, the inclusion of hydrophobic components in the compositions taught by Hoffman does not indicate that the compositions are distinct from those instantly claimed. Second, Hoffman clearly teaches that the hydrophilic component, i.e. PEG, can be covalently linked to an oligonucleotide drug via an acetal bond. Column 4, lines 32-39 of Hoffman read "In another embodiment, the hydrophilic groups are PEG groups, which are conjugated directly to drug molecules". At lines 40-51, Hoffman indicates that drugs include antisense oligodeoxynucleotides and that the drugs may be linked to either hydrophilic or hydrophobic components via an acetal bond. Applicant's conclusion, that the Hoffman composition is distinct from the instantly claimed composition and has a distinct mechanism of action from the instantly claimed composition such that one of skill in the art could not have looked to Hoffman and predicted the result of the present invention is not persuasive. The claims are directed to compositions that are not distinct from the instantly claimed compositions as indicated and further, the instant claims do not have functional limitations to distinguish the claimed compositions from those taught by Hoffman.

Hoffman, et al. and Tullis, et al.

Claims 1-4 and 6-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hoffman, et al. (US Patent 7,737,108, filed 01/05/2001, of record) as applied to claims 1, 2, 4, 6, 7, 9, and 10 above, and further in view of Tullis (1990, US Patent 4,904,582, of record). This

rejection is maintained.

Claims 1, 2, 4, 6, 7, 9, and 10 are described above. Claim 8 is to a conjugate for gene transfer comprising a hydrophilic polymer and an antisense oligonucleotide comprising a nucleotide sequence complementary to a portion or entire nucleotide sequence of the c-myc gene.

Hoffman, et al. render claims 1, 2, 4, 6, 7, 9, and 10 obvious for the reasons presented in the preceding rejection. Hoffman, et al. does not teach the antisense oligonucleotide-hydrophilic polymer conjugate wherein the antisense oligonucleotide is complementary to a portion or to the entire nucleotide sequence of the c-myc gene (instant claim 8) or wherein the antisense oligonucleotide has a molecular weight ranging from 1000-50000 daltons (instant claim 3).

Tullis describes oligonucleotide conjugates for transport across cellular membranes for modulating gene expression (abstract). In Table 1 in column 19, Tullis discloses the "MBF 20 antisense C_2-PEG" probe that comprises a 20-nucleotide phosphodiester-linked molecule conjugated to PEG (M_r = 3500). Such a probe is complementary to a portion of the c-myc gene. Tullis teaches that the PEG group can be added to 5'- or 3'-end of the antisense oligonucleotide by various protocols (column 5, line 44 to column 6 line 8). According to the website, www.newton.dep.anl.gov (of record), a 20-nucleotide single-stranded DNA molecule has a molecular weight of approximately 6600 daltons (330 daltons per nucleotide).

It would have been obvious to one of skill in the art at the time the instant invention was made to make an antisense-PEG conjugate wherein the antisense oligonucleotide comprises a sequence that is complementary to a portion of the c-myc gene and wherein the PEG is conjugated to the oligonucleotide via an acetal bond because Tullis, et al. teaches antisense

oligonucleotide-PEG conjugates wherein the oligonucleotide comprises a sequence having complementarity to a portion of the c-myc gene and Hoffman, et al. teach that antisense oligonucleotides can be conjugated to PEG via an acetal bond.

Response to arguments

Applicant argues that Hoffman does not teach or provide any reason for a conjugate comprising an oligonucleotide and a hydrophilic polymer, wherein the end of the oligonucleotide is covalently linked to the hydrophilic polymer via an acid-cleavable linkage (page 4 of 10/01/2010 response). This is not persuasive for the reasons indicated in the response to arguments to the previous rejection. Applicant argues that Tullis does not remedy the deficiencies of Hoffman and, therefore, a prima facie case of obviousness has not been established. This is not persuasive for the reasons indicated in the response to arguments to the previous rejection.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re

Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 2, 3, 4, 6, 7, 8, 9, and 10 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 3, 8, 10, and 13 of copending Application No. 11/651011 in view of Hoffman, et al. (US Patent 7,737,108, filed 01/05/2001, of record)

The instant claims are directed to a composition comprising an oligonucleotide and a hydrophilic polymer wherein an end of the oligonucleotide is covalently linked to the hydrophilic polymer via an acid-cleavable linkage, which is an acetal bond. Claim 4 specifies that the hydrophilic polymer can be PEG. Claim 2 specifies that the hydrophilic polymer has a molecular weight of over 500 daltons. Claim 3 specifies that the oligonucleotide has a molecular

weight ranging from 1000 to 50000 daltons. Claims 7 and 8 specify that the oligonucleotide is a c-myc-targeted antisense oligonucleotide.

The claims of the 11/651011 application are directed to a composition comprising a c-myc-targeted siRNA and a hydrophilic polymer (PEG) wherein an end of the siRNA is covalently linked to a hydrophilic polymer via an acid-cleavable linkage. The siRNAs encompassed by the '011 claims include those having a molecular weight of 10,000 to 30,000 (paragraph 15) and the PEG of the '011 claims includes that having a molecular weight of between 1000 to 10,000 (see original claim 2 of the '011 application). The '011 claims and specification do not specify that the acid cleavable linkage is an acetal bond.

Hoffman teaches conjugation of antisense oligonucleotides and PEG via an acetal bond.

The instant claims would have been prima facie obvious to one of skill in the art provided with the claims of the 11/651011 application and the teachings of Hoffman, et al. Aside from the limitation of an acetal bond in the instant claims, the siRNA-PEG complex of the '011 application is a species of the instantly claimed oligonucleotide-PEG complex. Hoffman, et al. provide the teaching that an acetal bond is a preferred acid-cleavable linkage for conjugating PEG and oligonucleotides (see rejection under 35 USC § 103, above) such that one of skill in the art would recognize that the acid-cleavable linkage specified in the '011 claims include an acetal bond and that such a bond is preferred, according to Hoffman. One of skill in the art would also recognize that the c-myc-targeted siRNA of the '011 application claims could be substituted with the instantly claimed c-myc-targeted antisense oligonucleotide because both molecules are known gene expression inhibitors. Therefore, the instant claims would have been prima facie obvious to one of skill in the art provided with the '011 claims and the teachings of Hoffman.

This is a provisional obviousness-type double patenting rejection.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JENNIFER PITRAK whose telephone number is (571)270-3061. The examiner can normally be reached on Monday-Friday, 8:30AM-5:00PM, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Heather Calamita can be reached on 571-272-2876. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jennifer Pitrak/
Examiner, Art Unit 1635